

PTO 09-0141

CC=CN DATE=20040220 KIND=Patent
PN=200410021172.3

SUBSTITUED AZOLE COMPOUNDS AND THE PREPARATION AND APPLICATION THEREOF
[Qu Dai Zuo Lei Hua He Wu ji qi Zhi Bei yu Ying Yong]

CHANGLING LIU, et al.

UNITED STATES PATENT AND TRADEMARK OFFICE
Washington, D.C. October 2008

Translated by: FLS, Inc.

PUBLICATION COUNTRY	(19):	CN
DOCUMENT NUMBER	(11):	
DOCUMENT KIND	(12):	PATENT
PUBLICATION DATE	(43):	
APPLICATION NUMBER	(21):	200410021172.3
DATE OF FILING	(22):	20040220
ADDITION TO	(61):	
INTERNATIONAL CLASSIFICATION	(51):	
PRIORITY	(30):	
INVENTORS	(72):	LIU, CHANGLING; LI, LIN; ZHANG, HONG; LI, MIAO; ZHANG, MINGXING; GUAN, AIYING; HOU, CHUNQING; LI, ZHINIAN
APPLICANT	(71):	SHENYANG RESEARCH INSTITUTE OF CHEMICAL INDUSTRY
DESIGNATED CONTRACTING STATES	(81):	
TITLE	(54):	SUBSTITUED AZOLE COMPOUNDS AND THE PREPARATION AND APPLICATION THEREOF
FOREIGN TITLE	[54A]:	QU DAI ZUO LEI HUA HE WU JI QI ZHI BEI YU YING YONG

Chemical structure (I) is a pyrazole derivative. The pyrazole ring is substituted at the 2-position with a pyridine ring (labeled A₁, A₂, A₃) and at the 3-position with a benzene ring (labeled R₂). The pyrazole ring also has substituents R₄ and R₅ at the 4 and 5 positions, respectively. The pyrazole ring is linked via an oxygen atom to a benzene ring (labeled R₂). The benzene ring is substituted with a carbonyl group (C=O) and an ether group (O-R). The carbonyl group is linked to a substituent R₁ via a bond labeled X₂. The ether group is linked to a substituent R via a bond labeled X₁. The pyrazole ring is also linked to a substituent R₃ via a bond labeled X₃.

R₁ and R₂ are selected from C₁ - C₁₂ alkyl or C₁ - C₁₂ haloalkyl, respectively; R₃ is selected from hydrogen, halogen atoms, C₁ - C₁₂ alkyl, C₁ - C₁₂ haloalkyl, or C₁ - C₁₂ alkoxy; R₇ is selected from hydrogen or (C₁ - C₁₂) alkyl; R₈ is selected from hydrogen, C₁ - C₁₂ alkyl, C₁ - C₁₂ haloalkyl, C₁ - C₁₂ alkoxycarbonyl or C₁ - C₁₂ alkoxycarbonyl C₁ - C₁₂ alkyl; R₄, R₅, R₆, R₉, R₁₀, and R₁₁ can be the same or different, and are selected from hydrogen, halogen atoms, a nitro group, a cyano group, CONH₂, CH₂CONH₂, CH₂CN, C₁ - C₁₂ alkyl, C₁ - C₁₂ haloalkyl, C₁ - C₁₂ alkoxy, C₁ - C₁₂ haloalkoxy,

2

C₁ - C₁₂ alkylthio, C₁ - C₁₂ alkylsulfonyl, C₁ - C₁₂ alkylcarbonyl, C₁ - C₁₂ alkoxy C₁ - C₁₂ alkyl, C₁ - C₁₂ alkoxycarbonyl, C₁ - C₁₂ alkoxycarbonyl C₁ - C₁₂ alkyl, and C₁ - C₁₂ haloalkoxy C₁ - C₁₂ alkyl, respectively; any of the following groups may be substituted: amino C₁ - C₁₂ alkyl, aryl, heteroaryl, aroxyl, aryl C₁ - C₁₂ alkyl, aryl C₁ - C₁₂ alkoxy, heteroaryl C₁ - C₁₂ alkyl, and heteroaryl C₁ - C₁₂ alkoxy, respectively.

2. A compound according to Claim 1 of the Patent Application Claims, wherein it is characterized by within General Formula (I):

X₁ is selected from CH or N, X₂ is selected from O, S or NR₇, and X₃ is selected from O, S or NR₈;

A₁, A₂, and A₃ are selected from CR₉, CR₁₀, and CR₁₁, respectively, or any A is selected from N;

R₁ and R₂ are selected from C₁ - C₆ alkyl or C₁ - C₆ haloalkyl, respectively; R₃ is selected from hydrogen, halogen atoms, C₁ - C₆ alkyl, C₁ - C₆ haloalkyl, or C₁ - C₆ alkoxy; R₇ is selected from hydrogen or (C₁ - C₆) alkyl; R₈ is selected from hydrogen, C₁ - C₆ alkyl, C₁ - C₆ haloalkyl, C₁ - C₆ alkoxycarbonyl or C₁ - C₆ alkoxycarbonyl C₁ - C₆ alkyl; R₄, R₅, R₆, R₉, R₁₀, and R₁₁ can be the same or different, and are selected from hydrogen, halogen atoms, a nitro group, a cyano group, CONH₂, CH₂CONH₂, CH₂CN, C₁ - C₆ alkyl, C₁ - C₆ haloalkyl, C₁ - C₆ alkoxy, C₁ - C₆ haloalkoxy, C₁ - C₆ alkylthio, C₁ - C₆ alkylsulfonyl, C₁ - C₆ alkylcarbonyl, C₁ - C₆ alkoxy C₁ - C₆ alkyl, C₁ - C₆ alkoxycarbonyl, C₁ - C₆ alkoxycarbonyl C₁ - C₆ alkyl, and C₁ - C₆ haloalkoxy C₁ - C₆ alkyl, respectively; any of the following groups may be substituted: amino C₁ - C₆ alkyl, aryl, heteroaryl, aroxyl, aryl C₁ - C₆ alkyl, aryl C₁ - C₆ alkoxy, heteroaryl C₁ - C₆ alkyl, and

heteroaryl C₁ - C₆ alkoxy, respectively.

3. A compound according to Claim 2 of the Patent Application Claims, wherein it is characterized by within General Formula (I):

X₁ is selected from CH or N, X₂ is selected from O or NH, and X₃ is selected from O or NR₈;

A₁, A₂, and A₃ are selected from CR₉, CR₁₀, and CR₁₁, respectively, /2 or any A is selected from N;

R₁ and R₂ are selected from methyl; R₃ is selected from hydrogen; R₈ is selected from hydrogen, C₁ - C₆ alkyl; C₁ - C₆ haloalkyl; C₁ - C₃ alkoxycarbonyl or C₁ - C₆ alkoxycarbonyl C₁ - C₃ alkyl; R₄, R₅, R₆, R₉, R₁₀, and R₁₁ can be the same or different, and are selected from hydrogen, halogen atoms, a nitro group, a cyano group, CONH₂, CH₂CONH₂, CH₂CN, C₁ - C₆ alkyl, C₁ - C₆ haloalkyl, C₁ - C₆ alkoxy, C₁ - C₆ haloalkoxy, C₁ - C₆ alkylthio, C₁ - C₆ alkylsulfonyl, C₁ - C₆ alkylcarbonyl, C₁ - C₆ alkoxy C₁ - C₆ alkyl, C₁ - C₆ alkoxycarbonyl, C₁ - C₆ alkoxycarbonyl C₁ - C₆ alkyl, and C₁ - C₆ haloalkoxy C₁ - C₆ alkyl, respectively; any of the following groups may be substituted: amino C₁ - C₃ alkyl, phenyl, benzyl, phenoxy, or benzyloxy, respectively.

4. A compound according to Claim 3 of the Patent Application Claims, wherein it is characterized by within General Formula (I):

X₁ is selected from CH or N, X₂ is selected from O or NH, and X₃ is selected from O or NR₈;

A₁, A₂, and A₃ are selected from CR₉, CR₁₀, and CR₁₁, respectively, or any of A₁ and A₂ are selected from N;

R₁ and R₂ are selected from methyl; R₃ is selected from hydrogen;

R₈ is selected from hydrogen, C₁ - C₃ alkyl, C₁ - C₃ haloalkyl, C₁ - C₃ alkoxy carbonyl, or C₁ - C₃ alkoxy carbonyl C₁ - C₃ alkyl; R₄, R₅, R₆, R₉, R₁₀, and R₁₁ can be the same or different, and are selected from hydrogen, chlorine, bromine, fluorine, a nitro group, a cyano group, C₁ - C₆ alkyl, C₁ - C₆ haloalkyl, C₁ - C₆ alkoxy, C₁ - C₆ alkyl carbonyl, C₁ - C₆ alkoxy C₁ - C₃ alkyl, C₁ - C₃ haloalkoxy C₁ - C₃ alkyl, amino C₁ - C₃ alkyl, phenyl, or benzyl, respectively.

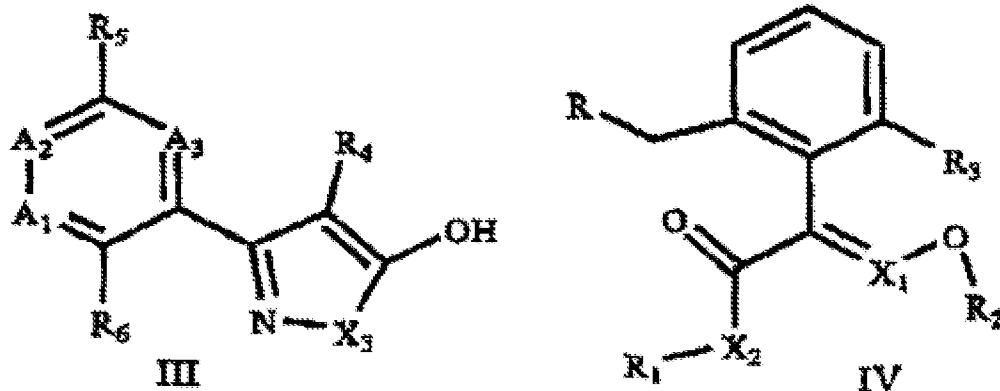
5. A compound according to Claim 4 of the Patent Application Claims, wherein it is characterized by within General Formula (I):

X₁ is selected from CH or N, X₂ is selected from O or NH, and X₃ is selected from O or NR₈;

A₁, A₂, and A₃ are selected from CR₉, CR₁₀, and CR₁₁, respectively, or any of A₁ and A₂ are selected from N;

R₁ and R₂ are selected from methyl; R₃ is selected from hydrogen; R₈ is selected from hydrogen, C₁ - C₃ alkyl, C₁ - C₃ haloalkyl, C₁ - C₃ alkoxy carbonyl, or C₁ - C₃ alkoxy carbonyl C₁ - C₃ alkyl; R₄, R₅, R₆, R₉, R₁₀, and R₁₁ can be the same or different, and are selected from hydrogen, chlorine, bromine, fluorine, a nitro group, a cyano group, C₁ - C₆ alkyl, C₁ - C₆ haloalkyl, C₁ - C₆ alkoxy, C₁ - C₆ alkyl carbonyl, C₁ - C₆ alkoxy C₁ - C₃ alkyl, and C₁ - C₃ haloalkoxy C₁ - C₃ alkyl.

6. A preparation method for General Formula (I) and the stereoisomer thereof as described in Claim 1 of the Patent Application Claims, wherein it is prepared by the reaction of the azole compound containing a hydroxyl group as shown in General Formula (III) with a benzyl halide as shown in General Formula (IV) under the presence of a base:



within General Formula (IV), R is a leaving group selected from chlorine or bromine; each of the other groups are as previously defined.

7. The application of the compound of General Formula (I) and the stereoisomer thereof for the use of preventing diseases in plants.

8. A composition of fungicide, wherein it is characterized by active ingredients of the compound of General Formula (I) and the stereoisomer thereof having a weight percentage of 0.1 - 99%.

DESCRIPTION OF THE INVENTION

/1

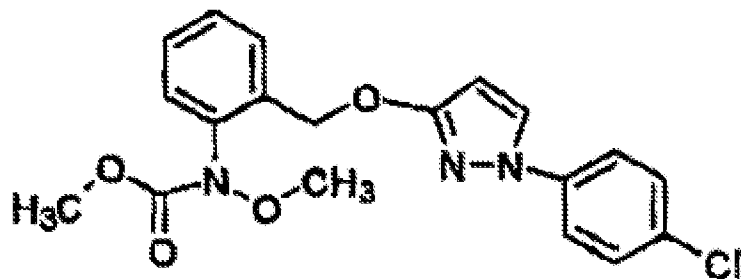
SUBSTITUTED AZOLE COMPOUNDS AND THE PREPARATION AND APPLICATION THEREOF

Technical Field

The present invention is related to fungicides for agricultural use.

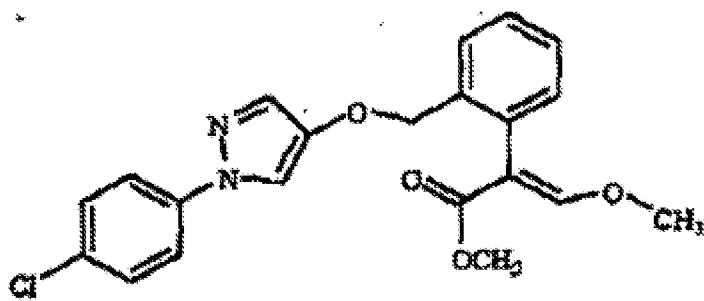
Background of the Invention

Naturally produced methoxyacrylate compounds are known to have biologically active compounds. The pyraclostrobin broad spectrum fungicide was already disclosed in patents US5869517, US6054592, CN1154692A, and CN1308065A. Its chemical structure is as follows:



Pyraclostrobin

Patent DE19548786 disclosed a compound with fungicidal activity as follows:



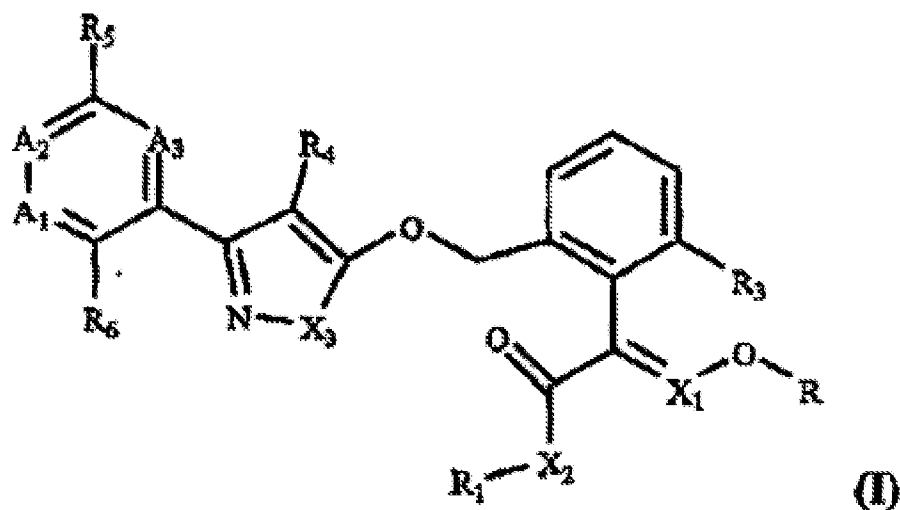
These compounds disclosed in the aforementioned patents are similar to the general formula compound structure presented in the present invention. However, there are still obvious differences.

Content of the Invention

In order to produce a new compound that can be used in lower dosages and provides improved biological activity to prevent all types of diseases, the inventors of the present invention synthesized a new class of substituted azole compound. Said azole compound provides broad-spectrum activity and can be used to prevent diseases caused by pathogens such as oomycete, basidiomycete, ascomycete, and deuteromycete. Moreover, because these compounds have very high biological activity, only a very low dosage is required to achieve optimal effectiveness. Said compounds

are very effective in preventing plant diseases such as cucumber downy mildew, cucumber grey mold, cucumber powdery mildew, tomato early blight, tomato late blight, phytophthora blight of pepper, grape downy mildew, grape white rot, apple ring rot, apple alternaria leaf spot, rice sheath blight, rice blast, wheat leaf rust, wheat leaf blotch, wheat powdery mildew, rape sclerotiniose, and corn southern leaf blight.

The new class of substituted azole compound provided by the /2
present invention and the stereoisomer thereof can be represented by General Formula (I):



wherein, within the formula:

X₁ is selected from CH or N, X₂ is selected from O, S or NR₇, and X₃ is selected from O, S or NR₈;

A₁, A₂, and A₃ are selected from CR₉, CR₁₀, and CR₁₁, respectively, or any A is selected from N;

R₁ and R₂ are selected from C₁ - C₁₂ alkyl or C₁ - C₁₂ haloalkyl, respectively; R₃ is selected from hydrogen, halogen atoms, C₁ - C₁₂ alkyl, C₁ - C₁₂ haloalkyl, or C₁ - C₁₂ alkoxy; R₇ is selected from hydrogen or

(C₁ - C₁₂) alkyl; R₈ is selected from hydrogen, C₁ - C₁₂ alkyl, C₁ - C₁₂ haloalkyl, C₁ - C₁₂ alkoxy, C₁ - C₁₂ haloalkoxy, C₁ - C₁₂ alkylthio, C₁ - C₁₂ alkylsulfonyl, C₁ - C₁₂ alkylcarbonyl, C₁ - C₁₂ alkoxy C₁ - C₁₂ alkyl, C₁ - C₁₂ alkoxy, C₁ - C₁₂ haloalkoxy, C₁ - C₁₂ alkylthio, C₁ - C₁₂ alkylsulfonyl, C₁ - C₁₂ alkylcarbonyl, C₁ - C₁₂ alkoxy C₁ - C₁₂ alkyl, C₁ - C₁₂ alkoxy, C₁ - C₁₂ haloalkoxy, C₁ - C₁₂ alkylthio, C₁ - C₁₂ alkylsulfonyl, C₁ - C₁₂ alkylcarbonyl, C₁ - C₁₂ alkoxy C₁ - C₁₂ alkyl, and C₁ - C₁₂ haloalkoxy C₁ - C₁₂ alkyl, respectively; any of the following groups may be substituted: amino C₁ - C₁₂ alkyl, aryl, heteroaryl, aroxy, aryl C₁ - C₁₂ alkyl, aryl C₁ - C₁₂ alkoxy, heteroaryl C₁ - C₁₂ alkyl, and heteroaryl C₁ - C₁₂ alkoxy, respectively.

The better suited compounds of the present invention are: within General Formula (I):

X₁ is selected from CH or N, X₂ is selected from O, S or NR₇, and X₃ is selected from O, S or NR₈;

A₁, A₂, and A₃ are selected from CR₉, CR₁₀, and CR₁₁, respectively, or any A is selected from N;

R₁ and R₂ are selected from C₁ - C₆ alkyl or C₁ - C₆ haloalkyl, respectively; R₃ is selected from hydrogen, halogen atoms, C₁ - C₆ alkyl, C₁ - C₆ haloalkyl, or C₁ - C₆ alkoxy; R₇ is selected from hydrogen or (C₁ - C₆) alkyl; R₈ is selected from hydrogen, C₁ - C₆ alkyl, C₁ - C₆ haloalkyl, C₁ - C₆ alkoxy, C₁ - C₆ haloalkoxy, C₁ - C₆ alkylthio, C₁ - C₆ alkylsulfonyl, C₁ - C₆ alkylcarbonyl, C₁ - C₆ alkoxy C₁ - C₆ alkyl, and C₁ - C₆ haloalkoxy C₁ - C₆ alkyl, respectively; R₄, R₅, R₆, R₉, R₁₀, and R₁₁ can be the same or different, and are selected from hydrogen, halogen atoms, a nitro group, a cyano group, CONH₂, CH₂CONH₂, CH₂CN, C₁ - C₆ alkyl, C₁ - C₆ haloalkyl, C₁ - C₆ alkoxy, C₁ - C₆ haloalkoxy, C₁ - C₆

alkylthio, C₁ - C₆ alkylsulfonyl, C₁ - C₆ alkylcarbonyl, C₁ - C₆ alkoxy C₁ - C₆ alkyl, C₁ - C₆ alkoxy carbonyl, C₁ - C₆ alkoxy carbonyl C₁ - C₆ alkyl, and C₁ - C₆ haloalkoxy C₁ - C₆ alkyl, respectively; any of the following groups may be substituted: amino C₁ - C₆ alkyl, aryl, heteroaryl, aroxyl, aryl C₁ - C₆ alkyl, aryl C₁ - C₆ alkoxy, heteroaryl C₁ - C₆ alkyl, and heteroaryl C₁ - C₆ alkoxy, respectively.

The preferred compounds of the aforementioned better suited compounds of the present invention are: within General Formula (I):

X₁ is selected from CH or N, X₂ is selected from O or NH, and X₃ /3 is selected from O or NR₈;

A₁, A₂, and A₃ are selected from CR₉, CR₁₀, and CR₁₁, respectively, or any A is selected from N;

R₁ and R₂ are selected from methyl; R₃ is selected from hydrogen; R₈ is selected from hydrogen, C₁ - C₆ alkyl, C₁ - C₆ haloalkyl, C₁ - C₃ alkoxy carbonyl or C₁ - C₆ alkoxy carbonyl C₁ - C₃ alkyl; R₄, R₅, R₆, R₉, R₁₀, and R₁₁ can be the same or different, and are selected from hydrogen, halogen atoms, a nitro group, a cyano group, CONH₂, CH₂CONH₂, CH₂CN, C₁ - C₆ alkyl, C₁ - C₆ haloalkyl, C₁ - C₆ alkoxy, C₁ - C₆ haloalkoxy, C₁ - C₆ alkylthio, C₁ - C₆ alkylsulfonyl, C₁ - C₆ alkylcarbonyl, C₁ - C₆ alkoxy C₁ - C₆ alkyl, C₁ - C₆ alkoxy carbonyl, C₁ - C₆ alkoxy carbonyl C₁ - C₆ alkyl, and C₁ - C₆ haloalkoxy C₁ - C₆ alkyl, respectively; any of the following groups may be substituted: amino C₁ - C₃ alkyl, phenyl, benzyl, phenoxy, or benzyloxy, respectively.

Further optimized compounds are: within General Formula (I):

X₁ is selected from CH or N, X₂ is selected from O or NH, and X₃ is

selected from O or NR₈;

A₁, A₂, and A₃ are selected from CR₉, CR₁₀, and CR₁₁, respectively, or any of A₁ and A₂ are selected from N;

R₁ and R₂ are selected from methyl; R₃ is selected from hydrogen; R₈ is selected from hydrogen, C₁ - C₃ alkyl, C₁ - C₃ haloalkyl, C₁ - C₃ alkoxy carbonyl, or C₁ - C₃ alkoxy carbonyl C₁ - C₃ alkyl; R₄, R₅, R₆, R₉, R₁₀, and R₁₁ can be the same or different, and are selected from hydrogen, chlorine, bromine, fluorine, a nitro group, a cyano group, C₁ - C₆ alkyl, C₁ - C₆ haloalkyl, C₁ - C₆ alkoxy, C₁ - C₆ alkyl carbonyl, C₁ - C₆ alkoxy C₁ - C₃ alkyl, C₁ - C₃ haloalkoxy C₁ - C₃ alkyl, amino C₁ - C₃ alkyl, phenyl, or benzyl, respectively.

And even further optimized compounds are: within General Formula (I):

X₁ is selected from CH or N, X₂ is selected from O or NH, and X₃ is selected from O or NR₈;

A₁, A₂, and A₃ are selected from CR₉, CR₁₀, and CR₁₁, respectively, or any of A₁ and A₂ are selected from N;

R₁ and R₂ are selected from methyl; R₃ is selected from hydrogen; R₈ is selected from hydrogen, C₁ - C₃ alkyl, C₁ - C₃ haloalkyl, C₁ - C₃ alkoxy carbonyl, or C₁ - C₃ alkoxy carbonyl C₁ - C₃ alkyl; R₄, R₅, R₆, R₉, R₁₀, and R₁₁ can be the same or different, and are selected from hydrogen, chlorine, bromine, fluorine, a nitro group, a cyano group, C₁ - C₆ alkyl, C₁ - C₆ haloalkyl, C₁ - C₆ alkoxy, C₁ - C₆ alkyl carbonyl, C₁ - C₆ alkoxy C₁ - C₃ alkyl, and C₁ - C₃ haloalkoxy C₁ - C₃ alkyl.

The collection of terms in the definition of the aforementioned

Compound (I) are generally represented by the following replacements:

Halogen: refers to fluoro, chloro, bromo, and iodo;

Alkyl: Either straight or branched chain alkyl such as methyl, ethyl, propyl, isopropyl, and tert-butyl;

Haloalkyl: Either straight or branched chain alkyl, in which the hydrogen atom of such alkyl may be all or partly substituted with halogen atoms, such as a haloalkyl including chloromethyl, dichloromethyl, trichloromethyl, fluoromethyl, difluoromethyl, and trifluoromethyl;

Alkoxy: Either straight or branched chain alkyl, which is linked to the structure via an oxygen atom;

Haloalkoxy: Either straight or branched chain alkoxy, in which the hydrogen atom may be all or partly substituted with halogen atoms, such as a haloalkoxy including chloromethoxy, dichloromethoxy, trichloromethoxy, fluoromethoxy, difluoromethoxy, trifluoromethoxy, chlorofluoromethoxy;

Alkenyl: Either straight or branched chains having double bonds at any position, such as vinyl or allyl. Substituted alkenyl includes arylvinyl which is substituted at any position with any group; /4

Alkynyl: Either straight or branched chains having triple bonds at any position, such as ethynyl, propynyl. Substituted alkynyl includes arylethynyl which is substituted at any position with any group.

The aryl and aryl in arylalkyl, arylalkenyl, arylalkynyl, aryloxy, aryloxyalkyl include phenyl and naphthyl.

(Substituted) phenoxy, (substituted) benzyloxy, (substituted) phenyl, and (substituted) benzyl can substituted with hydrogen, alkyl,

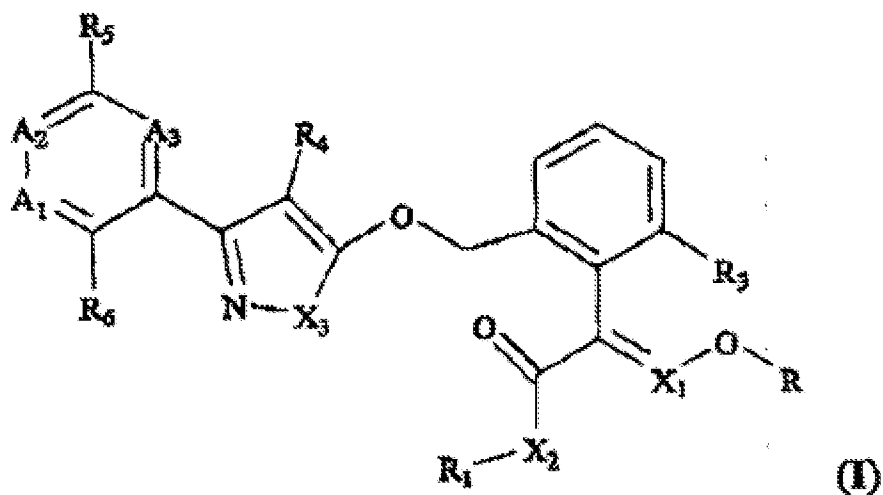
alkoxy, haloalkyl, haloalkoxy, hydrogen elements, nitro, CN, etc. The number of substitutions can be 0 - 5.

The hetero aryl of the present invention refers to a five member ring or a six member ring containing one or many N, O, S hetero atoms, such as pyridine, furan, pyrimidine, pyrazine, pyridazine, triazine, quinoline, and benzofuran.

Because of the double carbon-carbon and carbon-nitrogen links to different substituted groups, the compounds of the present invention may form geometrical isomers (the different structures are expressed with Z and E, respectively). Z isomers and E isomers and their mixture in any proportion are included in the present invention.

The present invention can be explained by the following compounds in Tables 1 - 3, but without limiting the present invention.

Table 1



Of which, R_1 and $R_2 = \text{CH}_3$, $R_3 = \text{H}$, $X_1 = \text{CH}$, and $X_2 = \text{O}$.

编号 ¹	X ₃	R ₄	R ₅	R ₆	A ₁	A ₂	A ₃
1	NCH ₃	H	H	H	CH	CH	CH
2	NCH ₃	H	H	H	CH	C-Cl	CH
3	NCH ₃	H	H	H	CH	C-F	CH
4	NCH ₃	H	H	H	CH	C-NO ₂	CH
5	NCH ₃	H	H	H	CH	C-CF ₃	CH
6	NCH ₃	H	H	H	CH	C-CN	CH
7	NCH ₃	H	H	H	CH	C-CH ₃	CH
8	NCH ₃	H	H	H	CH	C-OCH ₃	CH
9	NCH ₃	H	H	H	CH	C-OCF ₃	CH
10	NCH ₃	H	H	H	CH	C-Cl	C-Cl

11	NCH ₃	H	H	H	C-F	C-Cl	C-Cl
12	NCH ₃	H	H	H	C-OCH ₃	C-OCH ₃	CH
13	NCH ₃	H	H	H	CH	C-F	C-Cl
14	NCH ₃	H	Cl	H	C-Cl	CH	CH
15	NCH ₃	H	H	CH ₃	CH	C-CH ₃	CH
16	NCH ₃	Cl	H	H	CH	CH	CH
17	NCH ₃	Cl	H	H	CH	C-Cl	CH
18	NCH ₃	Cl	H	H	CH	C-F	CH
19	NCH ₃	Cl	H	H	CH	C-NO ₂	CH
20	NCH ₃	Cl	H	H	CH	C-CF ₃	CH
21	NCH ₃	Cl	H	H	CH	C-CN	CH
22	NCH ₃	Cl	H	H	CH	C-CO ₂ Me	CH
23	NCH ₃	Cl	H	H	CH	C-OCH ₃	CH
24	NCH ₃	Cl	H	H	CH	C-OCF ₃	CH
25	NCH ₃	Cl	H	H	CH	C-Cl	C-Cl
26	NCH ₃	Cl	H	H	C-F	C-Cl	C-Cl
27	NCH ₃	Cl	H	H	CH	C-F	C-Cl
28	NCH ₃	Cl	Cl	H	C-Cl	CH	CH
29	NCH ₃	CN	H	H	CH	CH	CH
30	NCH ₃	CN	H	H	CH	C-Cl	CH
31	NCH ₃	CN	H	H	CH	C-F	CH
32	NCH ₃	CN	H	H	CH	C-NO ₂	CH
33	NCH ₃	CN	H	H	CH	C-CF ₃	CH
34	NCH ₃	CN	H	H	CH	C-CN	CH
35	NCH ₃	OCH ₃	H	H	CH	C-CO ₂ Me	CH
36	NCH ₃	CN	H	H	CH	C-OCH ₃	CH
37	NCH ₃	CN	H	H	CH	C-OCF ₃	CH
38	NCH ₃	CN	H	H	CH	C-Cl	C-Cl
39	NCH ₃	CN	H	H	C-F	C-Cl	C-Cl
40	NCH ₃	CN	H	H	C-OCH ₃	C-OCH ₃	CH
41	NCH ₃	OCH ₃	H	H	CH	C-F	C-Cl
42	NCH ₃	OCH ₃	H	H	CH	C-Cl	CH
43	NCH ₃	CO ₂ Me	H	H	CH	CH	CH
44	NCH ₃	CO ₂ Me	H	H	CH	C-Cl	CH
45	NCH ₃	CO ₂ Me	H	H	CH	C-F	CH
46	NCH ₃	CO ₂ Me	H	H	CH	C-NO ₂	CH
47	NCH ₃	CO ₂ Me	H	H	CH	C-CF ₃	CH
48	NCH ₃	CO ₂ Me	H	H	CH	C-CN	CH
49	NCH ₃	CO ₂ Me	H	H	CH	C-CO ₂ Me	CH
50	NCH ₃	CO ₂ Me	H	H	CH	C-OCH ₃	CH
51	NCH ₃	CO ₂ Me	H	H	CH	C-OCF ₃	CH
52	NCH ₃	CO ₂ Me	H	H	CH	C-Cl	C-Cl
53	NCH ₃	CO ₂ Me	H	H	C-F	C-Cl	C-Cl

54	NCH ₃	CO ₂ Me	H	H	C-OCH ₃	C-OCH ₃	CH
55	NCH ₃	CO ₂ Me	H	H	CH	C-F	C-Cl
56	NCH ₃	CO ₂ Me	Cl	H	C-Cl	CH	CH
57	NCH ₃	H	H	H	CH	CH	N
58	NCH ₃	H	H	H	CH	C-Cl	N
59	NCH ₃	H	H	H	CH	C-OCH ₃	N
60	NCH ₃	H	H	H	C-Cl	CH	N
61	NCH ₃	H	H	H	CH	C-CF ₃	N
62	NCH ₃	H	H	Cl	CH	C-CF ₃	N
63	NCH ₃	Cl	H	H	CH	CH	N
64	NCH ₃	Cl	H	H	CH	C-Cl	N
65	NCH ₃	Cl	H	H	CH	C-OCH ₃	N
66	NCH ₃	Cl	H	H	C-Cl	CH	N
67	NCH ₃	Cl	H	H	CH	C-CF ₃	N
68	NCH ₃	Cl	H	Cl	CH	C-CF ₃	N
69	NCH ₃	H	H	H	N	C-Cl	CH
70	NCH ₃	H	H	H	N	C-F	CH
71	NCH ₃	H	H	H	N	C-OCF ₃	CH
72	NCH ₃	H	H	H	N	C-CF ₃	CH
73	NCH ₃	H	H	H	N	C-OCH ₃	CH
74	NCH ₃	H	H	H	N	C-OCH ₂ CF ₃	CH
75	NCH ₃	Cl	H	H	N	C-Cl	CH
76	NCH ₃	Cl	H	H	N	C-F	CH
77	NCH ₃	Cl	H	H	N	C-OCF ₃	CH
78	NCH ₃	Cl	H	H	N	C-CF ₃	CH
79	NCH ₃	Cl	H	H	N	C-OCH ₃	CH
80	NCH ₃	Cl	H	H	N	C-OCH ₂ CF ₃	CH
81	NCH ₃	H	H	H	CH	N	CH
82	NCH ₃	Cl	H	H	CH	N	CH
83	O	H	H	H	CH	CH	CH
84	O	H	H	H	CH	C-Cl	CH
85	O	H	H	H	CH	C-F	CH
86	O	H	H	H	CH	C-NO ₂	CH
87	O	H	H	H	CH	C-CF ₃	CH
88	O	H	H	H	CH	C-CN	CH
89	O	H	H	H	CH	C-CO ₂ Me	CH
90	O	H	H	H	CH	C-OCH ₃	CH
91	O	H	H	H	CH	C-OCF ₃	CH
92	O	H	H	H	CH	C-Cl	C-Cl
93	O	H	H	H	C-F	C-Cl	C-Cl
94	O	H	H	H	C-OCH ₃	C-OCH ₃	CH
95	O	H	H	H	CH	C-F	C-Cl
96	O	H	Cl	H	C-Cl	CH	CH

97	O	Cl	H	H	CH	CH	CH
98	O	Cl	H	H	CH	C-Cl	CH
99	O	Cl	H	H	CH	C-F	CH
100	O	Cl	H	H	CH	C-NO ₂	CH
101	O	Cl	H	H	CH	C-CF ₃	CH
102	O	Cl	H	H	CH	C-CN	CH
103	O	Cl	H	H	CH	C-CO ₂ Me	CH
104	O	Cl	H	H	CH	C-OCH ₃	CH
105	O	Cl	H	H	CH	C-OCF ₃	CH
106	O	Cl	H	H	CH	C-Cl	C-Cl
107	O	Cl	H	H	C-F	C-Cl	C-Cl
108	O	Cl	H	H	C-OCH ₃	C-OCH ₃	CH
109	O	Cl	H	H	CH	C-F	C-Cl
110	O	Cl	Cl	H	C-Cl	CH	CH
111	O	CN	H	H	CH	CH	CH
112	O	CN	H	H	CH	C-Cl	CH
113	O	CN	H	H	CH	C-F	CH
114	O	CN	H	H	CH	C-NO ₂	CH
115	O	CN	H	H	CH	C-CF ₃	CH
116	O	CN	H	H	CH	C-CN	CH
117	O	CN	H	H	CH	C-CO ₂ Me	CH
118	O	CN	H	H	CH	C-OCH ₃	CH
119	O	CN	H	H	CH	C-OCF ₃	CH
120	O	CN	H	H	CH	C-Cl	C-Cl
121	O	CN	H	H	C-F	C-Cl	C-Cl
122	O	OCH ₃	H	H	CH	C-Cl	CH
123	O	OCH ₃	H	H	CH	C-F	CH
124	O	OCH ₃	H	H	CH	C-CF ₃	CH
125	O	CO ₂ Me	H	H	CH	CH	CH
126	O	CO ₂ Me	H	H	CH	C-Cl	CH
127	O	CO ₂ Me	H	H	CH	C-F	CH
128	O	CO ₂ Me	H	H	CH	C-NO ₂	CH
129	O	CO ₂ Me	H	H	CH	C-CF ₃	CH
130	O	CO ₂ Me	H	H	CH	C-CN	CH
131	O	CO ₂ Me	H	H	CH	C-CO ₂ Me	CH
132	O	CO ₂ Me	H	H	CH	C-OCH ₃	CH
133	O	CO ₂ Me	H	H	CH	C-OCF ₃	CH
134	O	CO ₂ Me	H	H	CH	C-Cl	C-Cl
135	O	CO ₂ Me	H	H	C-F	C-Cl	C-Cl
136	O	CO ₂ Me	H	H	C-OCH ₃	C-OCH ₃	CH
137	O	CO ₂ Me	H	H	CH	C-F	C-Cl
138	O	CO ₂ Me	Cl	H	C-Cl	CH	CH
139	O	H	H	H	CH	CH	N

140	O	H	H	H	CH	C-Cl	N
141	O	H	H	H	CH	C-OCH ₃	N
142	O	H	H	H	C-Cl	CH	N
143	O	H	H	H	CH	C-CF ₃	N
144	O	H	H	Cl	CH	C-CF ₃	N
145	O	Cl	H	H	CH	CH	N
146	O	Cl	H	H	CH	C-Cl	N
147	O	Cl	H	H	CH	C-OCH ₃	N
148	O	Cl	H	H	C-Cl	CH	N
149	O	Cl	H	H	CH	C-CF ₃	N
150	O	Cl	H	Cl	CH	C-CF ₃	N
151	O	H	H	H	N	C-Cl	CH
152	O	H	H	H	N	C-F	CH
153	O	H	H	H	N	C-OCF ₃	CH
154	O	H	H	H	N	C-CF ₃	CH
155	O	H	H	H	N	C-OCH ₃	CH
156	O	H	H	H	N	C-OCH ₂ CF ₃	CH
157	O	Cl	H	H	N	C-Cl	CH
158	O	Cl	H	H	N	C-F	CH
159	O	Cl	H	H	N	C-OCF ₃	CH
160	O	Cl	H	H	N	C-CF ₃	CH
161	O	Cl	H	H	N	C-OCH ₃	CH
162	O	Cl	H	H	N	C-OCH ₂ CF ₃	CH
163	O	H	H	H	CH	N	CH
164	O	Cl	H	H	CH	N	CH
165	NEt	H	H	H	CH	CH	CH
166	NH	H	H	H	CH	C-Cl	CH
167	NH	H	H	H	CH	C-F	CH
168	NH	H	H	H	CH	C-NO ₂	CH
169	NH	H	H	H	CH	C-CF ₃	CH
170	NH	H	H	H	CH	C-CN	CH
171	NH	H	H	H	CH	C-CO ₂ Me	CH
172	NH	H	H	H	CH	C-OCH ₃	CH
173	NH	H	H	H	CH	C-OCF ₃	CH
174	NH	H	H	H	CH	C-Cl	C-Cl
175	NH	H	H	H	C-F	C-Cl	C-Cl
176	NEt	H	H	H	CH	C-Cl	CH
177	NH	H	H	H	CH	C-F	C-Cl
178	NH	H	Cl	H	C-Cl	CH	CH
179	NH	Cl	H	H	CH	CH	CH
180	NH	Cl	H	H	CH	C-Cl	CH
181	NH	Cl	H	H	CH	C-F	CH
182	NH	Cl	H	H	CH	C-NO ₂	CH

183	NH	Cl	H	H	CH	C-CF ₃	CH
184	NH	Cl	H	H	CH	C-CN	CH
185	NH	Cl	H	H	CH	C-CO ₂ Me	CH
186	NH	Cl	H	H	CH	C-OCH ₃	CH
187	NH	Cl	H	H	CH	C-OCF ₃	CH
188	NH	Cl	H	H	CH	C-Cl	C-Cl
189	NH	Cl	H	H	C-F	C-Cl	C-Cl
190	NPri	Cl	H	H	CH	C-Cl	CH
191	NH	Cl	H	H	CH	C-F	C-Cl
192	NH	Cl	Cl	H	C-Cl	CH	CH
193	NH	CN	H	H	CH	CH	CH
194	NH	CN	H	H	CH	C-Cl	CH
195	NH	CN	H	H	CH	C-F	CH
196	NH	CN	H	H	CH	C-NO ₂	CH
197	NH	CN	H	H	CH	C-CF ₃	CH
198	NH	CN	H	H	CH	C-CN	CH
199	NH	CN	H	H	CH	C-CO ₂ Me	CH
200	NH	CN	H	H	CH	C-OCH ₃	CH
201	NH	CN	H	H	CH	C-OCF ₃	CH
202	NH	CN	H	H	CH	C-Cl	C-Cl
203	NH	CN	H	H	C-F	C-Cl	C-Cl
204	NH	CN	H	H	C-OCH ₃	C-OCH ₃	CH
205	NH	OCH ₃	H	H	CH	C-F	CH
206	NH	OCH ₃	H	H	CH	C-Cl	CH
207	NH	CO ₂ Me	H	H	CH	CH	CH
208	NH	CO ₂ Me	H	H	CH	C-Cl	CH
209	NH	CO ₂ Me	H	H	CH	C-F	CH
210	NH	CO ₂ Me	H	H	CH	C-NO ₂	CH
211	NH	CO ₂ Me	H	H	CH	C-CF ₃	CH
212	NH	CO ₂ Me	H	H	CH	C-CN	CH
213	NH	CO ₂ Me	H	H	CH	C-CO ₂ Me	CH
214	NH	CO ₂ Me	H	H	CH	C-OCH ₃	CH
215	NH	CO ₂ Me	H	H	CH	C-OCF ₃	CH
216	NH	CO ₂ Me	H	H	CH	C-Cl	C-Cl
217	NH	CO ₂ Me	H	H	C-F	C-Cl	C-Cl
218	NH	CO ₂ Me	H	H	C-OCH ₃	C-OCH ₃	CH
219	NH	CO ₂ Me	H	H	CH	C-F	C-Cl
220	NH	CO ₂ Me	Cl	H	C-Cl	CH	CH
221	NH	H	H	H	CH	CH	N
222	NH	H	H	H	CH	C-Cl	N
223	NH	H	H	H	CH	C-OCH ₃	N
224	NH	H	H	H	C-Cl	CH	N
225	NH	H	H	H	CH	C-CF ₃	N

226	NH	H	H	Cl	CH	C-CF ₃	N
227	NH	Cl	H	H	CH	CH	N
228	NH	Cl	H	H	CH	C-Cl	N
229	NH	Cl	H	H	CH	C-OCH ₃	N
230	NH	Cl	H	H	C-Cl	CH	N
231	NH	Cl	H	H	CH	C-CF ₃	N
232	NH	Cl	H	Cl	CH	C-CF ₃	N
233	NH	H	H	H	N	C-Cl	CH
234	NH	H	H	H	N	C-F	CH
235	NH	H	H	H	N	C-OCF ₃	CH
236	NH	H	H	H	N	C-CF ₃	CH
237	NH	H	H	H	N	C-OCH ₃	CH
238	NH	H	H	H	N	C-OCH ₂ CF ₃	CH
239	NH	Cl	H	H	N	C-Cl	CH
240	NH	Cl	H	H	N	C-F	CH
241	NH	Cl	H	H	N	C-OCF ₃	CH
242	NH	Cl	H	H	N	C-CF ₃	CH
243	NH	Cl	H	H	N	C-OCH ₃	CH
244	NH	Cl	H	H	N	C-OCH ₂ CF ₃	CH
245	NH	H	H	H	CH	N	CH
246	NH	Cl	H	H	CH	N	CH

Key: 1) No.

The Physical and chemical properties and nuclear magnetic data (¹HNMR, 300 MHz, internal standard TMS, CDCl₃) of some of the compounds are as follows:

Compound 1:

123-127°C, δ ppm 7.73-7.21 (m, 10H, Ar-H) 5.78 (s, 1H, Het-H), 5.04 (s, 2H, CH₂), 3.84 (s, 3H, NCH₃), 3.71 (s, 6H, 2OCH₃).

Compound 2: viscous oil,

δ ppm 7.61-7.16 (m, 9H, Ar-H), 5.67 (s, 1H, Het-H), 5.09 (s, 2H, CH₂), 3.82 (s, 3H, NCH₃), 3.71 (s, 3H, OCH₃), 3.69 (s, 3H, OCH₃).

Compound 3:

107-109°C, δ ppm 7.71-7.02 (m, 9H, Ar-H) 5.73 (s, 1H, Het-H), 5.04 (s, 2H, CH₂), 3.84 (s, 3H, NCH₃), 3.71 (s, 6H, 2OCH₃).

Compound 4:

162-164°C, δ ppm 8.66-7.27 (m, 8H, Ar-H), 5.85 (s, 1H, Het-H), 5.06 (s, 2H, CH₂), 3.85 (s, 3H, NCH₃), 3.73 (s, 3H, OCH₃), 3.72 (s, 3H, OCH₃).

Compound 5: viscous oil,

δ ppm 7.75-7.16 (m, 9H, Ar-H), 5.73 (s, 1H, Het-H), 5.11 (s, 2H, CH₂), 3.82 (s, 3H, NCH₃), 3.74 (s, 3H, OCH₃) 3.69 (s, 3H, OCH₃).

Compound 12: viscous oil.

Compound 69:

137-140°C, δ ppm 8.30-7.27 (m, 8H, Ar-H), 5.79 (s, 1H, Het-H), 5.06 (s, 2H, CH₂), 3.85 (s, 3H, NCH₃), 3.73 (s, 3H, OCH₃), 3.72 (s, 3H, OCH₃).

Compound 83: viscous oil,

δ ppm 7.78-7.15 (m, 10H, Ar-H), 5.46 (s, 1H, Het-H), 5.18 (s, 2H, CH₂), 3.85 (s, 3H, OCH₃), 3.72 (s, 3H, OCH₃).

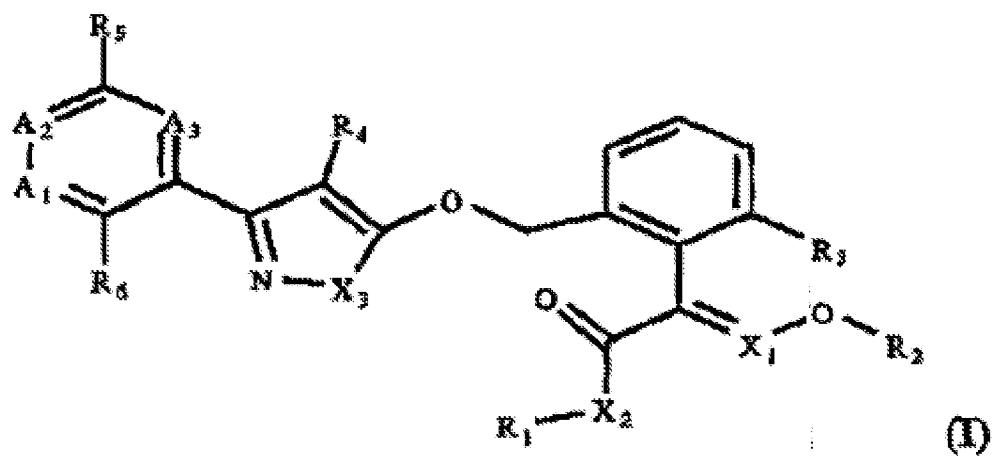
Compound 84: viscous oil.

Compound 86: 137-140°C, δ ppm 8.22-7.20 (m, 9H, Ar-H), 5.54 (s, 1H, Het-H),

5.21 (s, 2H, CH₂), 3.86 (s, 3H, OCH₃), 3.74 (s, 3H, OCH₃).

/11

Table 2



Of which, R_1 and $R_2 = \text{CH}_3$, $R_3 = \text{H}$, $X_1 = \text{N}$, and $X_2 = \text{O}$.

编号 ¹	X ₁	R ₄	R ₅	R ₆	A ₁	A ₂	A ₃
247	NCH ₃	H	H	H	CH	CH	CH
248	NCH ₃	H	H	H	CH	C-Cl	CH
249	NCH ₃	H	H	H	CH	C-F	CH
250	NCH ₃	H	H	H	CH	C-NO ₂	CH
251	NCH ₃	H	H	H	CH	C-CF ₃	CH
252	NCH ₃	H	H	H	CH	C-CN	CH
253	NCH ₃	H	H	H	CH	C-CO ₂ Me	CH
254	NCH ₃	H	H	H	CH	C-OCH ₃	CH
255	NCH ₃	H	H	H	CH	C-OCF ₃	CH
256	NCH ₃	H	H	H	CH	C-Cl	C-Cl
257	NCH ₃	H	H	H	C-F	C-Cl	C-Cl
258	NCH ₃	H	H	H	C-OCH ₃	C-OCH ₃	CH
259	NCH ₃	H	H	H	CH	C-F	C-Cl
260	NCH ₃	H	Cl	H	C-Cl	CH	CH
261	NCH ₃	Cl	H	H	CH	CH	CH
262	NCH ₃	Cl	H	H	CH	C-Cl	CH
263	NCH ₃	Cl	H	H	CH	C-F	CH
264	NCH ₃	Cl	H	H	CH	C-NO ₂	CH
265	NCH ₃	Cl	H	H	CH	C-CF ₃	CH
266	NCH ₃	Cl	H	H	CH	C-CN	CH
267	NCH ₃	Cl	H	H	CH	C-CO ₂ Me	CH
268	NCH ₃	Cl	H	H	CH	C-OCH ₃	CH
269	NCH ₃	Cl	H	H	CH	C-OCF ₃	CH
270	NCH ₃	Cl	H	H	CH	C-Cl	C-Cl
271	NCH ₃	Cl	H	H	C-F	C-Cl	C-Cl
272	NCH ₃	Cl	H	H	C-OCH ₃	C-OCH ₃	CH

273	NCH ₃	Cl	H	H	CH	C-F	C-Cl
274	NCH ₃	Cl	Cl	H	C-Cl	CH	CH
275	NCH ₃	H	H	H	CH	CH	N
276	NCH ₃	H	H	H	CH	C-Cl	N
277	NCH ₃	H	H	H	CH	C-OCH ₃	N
278	NCH ₃	H	H	H	C-Cl	CH	N
279	NCH ₃	H	H	H	CH	C-CF ₃	N
280	NCH ₃	H	H	Cl	CH	C-CF ₃	N
281	NCH ₃	Cl	H	H	CH	CH	N
282	NCH ₃	Cl	H	H	CH	C-Cl	N
283	NCH ₃	Cl	H	H	CH	C-OCH ₃	N
284	NCH ₃	Cl	H	H	C-Cl	CH	N
285	NCH ₃	Cl	H	H	CH	C-CF ₃	N
286	NCH ₃	Cl	H	Cl	CH	C-CF ₃	N
287	NCH ₃	H	H	H	N	C-Cl	CH
288	NCH ₃	H	H	H	N	C-F	CH
289	NCH ₃	H	H	H	N	C-OCF ₃	CH
290	NCH ₃	H	H	H	N	C-CF ₃	CH
291	NCH ₃	H	H	H	N	C-OCH ₃	CH
292	NCH ₃	H	H	H	N	C-OCH ₂ CF ₃	CH
293	NCH ₃	Cl	H	H	N	C-Cl	CH
294	NCH ₃	Cl	H	H	N	C-F	CH
295	NCH ₃	Cl	H	H	N	C-OCF ₃	CH
296	NCH ₃	Cl	H	H	N	C-CF ₃	CH
297	NCH ₃	Cl	H	H	N	C-OCH ₃	CH
298	NCH ₃	Cl	H	H	N	C-OCH ₂ CF ₃	CH
299	NCH ₃	H	H	H	CH	N	CH
300	NCH ₃	Cl	H	H	CH	N	CH
301	O	H	H	H	CH	CH	CH
302	O	H	H	H	CH	C-Cl	CH
303	O	H	H	H	CH	C-F	CH
304	O	H	H	H	CH	C-NO ₂	CH
305	O	H	H	H	CH	C-CF ₃	CH
306	O	H	H	H	CH	C-CN	CH
307	O	H	H	H	CH	C-CO ₂ Me	CH
308	O	H	H	H	CH	C-OCH ₃	CH
309	O	H	H	H	CH	C-OCF ₃	CH
310	O	H	H	H	CH	C-Cl	C-Cl
311	O	H	H	H	C-F	C-Cl	C-Cl
312	O	H	H	H	C-OCH ₃	C-OCH ₃	CH
313	O	H	H	H	CH	C-F	C-Cl
314	O	H	Cl	H	C-Cl	CH	CH
315	O	Cl	H	H	CH	CH	CH

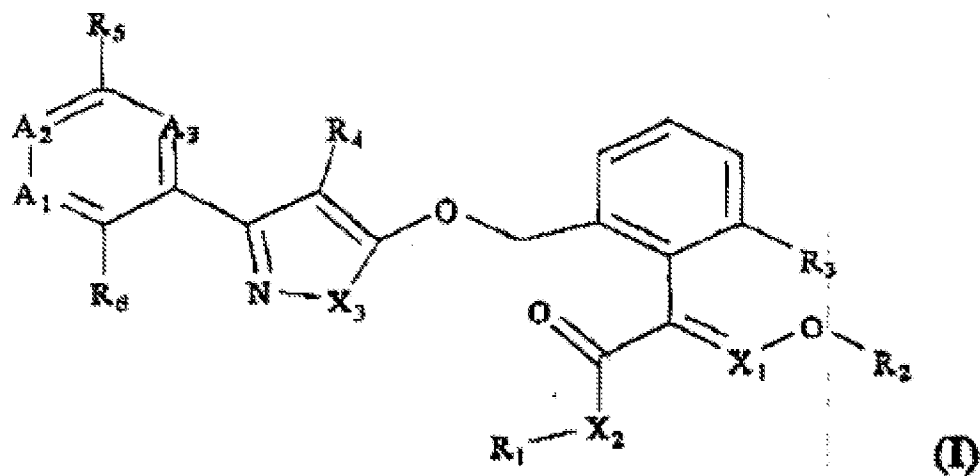
316	O	Cl	H	H	CH	C-Cl	CH
317	O	Cl	H	H	CH	C-F	CH
318	O	Cl	H	H	CH	C-NO ₂	CH
319	O	Cl	H	H	CH	C-CF ₃	CH
320	O	Cl	H	H	CH	C-CN	CH
321	O	Cl	H	H	CH	C-CO ₂ Me	CH
322	O	Cl	H	H	CH	C-OCH ₃	CH
323	O	Cl	H	H	CH	C-OCF ₃	CH
324	O	Cl	H	H	CH	C-Cl	C-Cl
325	O	Cl	H	H	C-F	C-Cl	C-Cl
326	O	Cl	H	H	C-OCH ₃	C-OCH ₃	CH
327	O	Cl	H	H	CH	C-F	C-Cl
328	O	Cl	Cl	H	C-Cl	CH	CH
329	O	H	H	H	CH	CH	N
330	O	H	H	H	CH	C-Cl	N
331	O	H	H	H	CH	C-OCH ₃	N
332	O	H	H	H	C-Cl	CH	N
333	O	H	H	H	CH	C-CF ₃	N
334	O	H	H	Cl	CH	C-CF ₃	N
335	O	Cl	H	H	CH	CH	N
336	O	Cl	H	H	CH	C-Cl	N
337	O	Cl	H	H	CH	C-OCH ₃	N
338	O	Cl	H	H	C-Cl	CH	N
339	O	Cl	H	H	CH	C-CF ₃	N
340	O	Cl	H	Cl	CH	C-CF ₃	N
341	O	H	H	H	N	C-Cl	CH
342	O	H	H	H	N	C-F	CH
343	O	H	H	H	N	C-OCF ₃	CH
344	O	H	H	H	N	C-CF ₃	CH
345	O	H	H	H	N	C-OCH ₃	CH
346	O	H	H	H	N	C-OCH ₂ CF ₃	CH
347	O	Cl	H	H	N	C-Cl	CH
348	O	Cl	H	H	N	C-F	CH
349	O	Cl	H	H	N	C-OCF ₃	CH
350	O	Cl	H	H	N	C-CF ₃	CH
351	O	Cl	H	H	N	C-OCH ₃	CH
352	O	Cl	H	H	N	C-OCH ₂ CF ₃	CH
353	O	H	H	H	CH	N	CH
354	O	Cl	H	H	CH	N	CH

Key: 1) No.

The melting point of Compound 287 is 141 - 143°C.

Table 3

/14



Of which, R₁ and R₂ = CH₃, R₃ = H, X₁ = N, and X₂ = NH.

编号 ¹	X ₃	R ₄	R ₅	R ₆	A ₁	A ₂	A ₃
355	NCH ₃	H	H	H	CH	CH	CH
356	NCH ₃	H	H	H	CH	C-Cl	CH
357	NCH ₃	H	H	H	CH	C-F	CH
358	NCH ₃	H	H	H	CH	C-NO ₂	CH
359	NCH ₃	H	H	H	CH	C-CF ₃	CH
360	NCH ₃	H	H	H	CH	C-CN	CH
361	NCH ₃	H	H	H	CH	C-OCF ₃	CH
362	NCH ₃	H	H	H	CH	C-Cl	C-Cl
363	NCH ₃	H	H	H	C-F	C-Cl	C-Cl
364	NCH ₃	H	Cl	H	C-Cl	CH	CH
365	NCH ₃	Cl	H	H	CH	CH	CH
366	NCH ₃	Cl	H	H	CH	C-Cl	CH
367	NCH ₃	Cl	H	H	CH	C-F	CH
368	NCH ₃	Cl	H	H	CH	C-NO ₂	CH
369	NCH ₃	Cl	H	H	CH	C-CF ₃	CH
370	NCH ₃	Cl	H	H	CH	C-CN	CH
371	NCH ₃	Cl	H	H	CH	C-OCF ₃	CH
372	NCH ₃	Cl	H	H	CH	C-Cl	C-Cl
373	NCH ₃	Cl	H	H	C-F	C-Cl	C-Cl
374	NCH ₃	Cl	Cl	H	C-Cl	CH	CH
375	O	H	H	H	CH	CH	CH
376	O	H	H	H	CH	C-Cl	CH
377	O	H	H	H	CH	C-F	CH
378	O	H	H	H	CH	C-NO ₂	CH
379	O	H	H	H	CH	C-CF ₃	CH
380	O	H	H	H	CH	C-CN	CH
381	O	H	H	H	CH	C-OCF ₃	CH
382	O	H	H	H	CH	C-Cl	C-Cl
383	O	H	H	H	C-F	C-Cl	C-Cl
384	O	H	Cl	H	C-Cl	CH	CH
385	O	Cl	H	H	CH	CH	CH

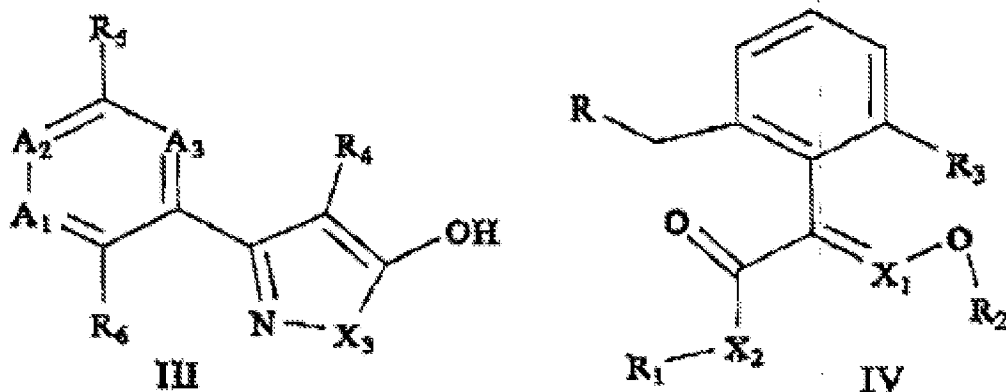
386	O	Cl	H	H	CH	C-Cl	CH
387	O	Cl	H	H	CH	C-F	CH
388	O	Cl	H	H	CH	C-NO ₂	CH
389	O	Cl	H	H	CH	C-CF ₃	CH
390	O	Cl	H	H	CH	C-CN	CH
391	O	Cl	H	H	CH	C-OCF ₃	CH
392	O	Cl	H	H	CH	C-Cl	C-Cl
393	O	Cl	H	H	C-F	C-Cl	C-Cl
394	O	Cl	Cl	H	C-Cl	CH	CH
395	NCH ₃	H	H	H	CH	CH	N
396	NCH ₃	H	H	H	CH	C-Cl	N
397	NCH ₃	H	H	H	CH	C-CF ₃	N
398	NCH ₃	H	H	Cl	CH	C-CF ₃	N
399	NCH ₃	Cl	H	H	CH	CH	N
400	NCH ₃	Cl	H	H	CH	C-Cl	N
401	NCH ₃	Cl	H	H	CH	C-CF ₃	N
402	NCH ₃	Cl	H	Cl	CH	C-CF ₃	N
403	NCH ₃	H	H	H	N	C-Cl	CH
404	NCH ₃	H	H	H	N	C-F	CH
405	NCH ₃	H	H	H	N	C-OCF ₃	CH
406	NCH ₃	H	H	H	N	C-CF ₃	CH
407	NCH ₃	H	H	H	N	C-OCH ₂ CF ₃	CH
408	NCH ₃	Cl	H	H	N	C-Cl	CH
409	NCH ₃	Cl	H	H	N	C-F	CH
410	NCH ₃	Cl	H	H	N	C-OCF ₃	CH
411	NCH ₃	Cl	H	H	N	C-CF ₃	CH
412	NCH ₃	Cl	H	H	N	C-OCH ₂ CF ₃	CH
413	NCH ₃	H	H	H	CH	N	CH
414	NCH ₃	Cl	H	H	CH	N	CH
415	O	H	H	H	CH	CH	N
416	O	H	H	H	CH	C-Cl	N
417	O	H	H	H	CH	C-CF ₃	N
418	O	H	H	Cl	CH	C-CF ₃	N
419	O	Cl	H	H	CH	CH	N
420	O	Cl	H	H	CH	C-Cl	N
421	O	Cl	H	H	CH	C-CF ₃	N
422	O	Cl	H	Cl	CH	C-CF ₃	N
423	O	H	H	H	N	C-Cl	CH
424	O	H	H	H	N	C-F	CH
425	O	H	H	H	N	C-OCF ₃	CH
426	O	H	H	H	N	C-CF ₃	CH
427	O	H	H	H	N	C-OCH ₂ CF ₃	CH
428	O	Cl	H	H	N	C-Cl	CH

429	O	Cl	H	H	N	C-F	CH
430	O	Cl	H	H	N	C-OCF ₃	CH
431	O	Cl	H	H	N	C-CF ₃	CH
432	O	Cl	H	H	N	C-OCH ₂ CF ₃	CH
433	O	H	H	H	CH	N	CH
434	O	Cl	H	H	CH	N	CH

Key: 1) No.

The present invention also includes preparation of the substituted azole compounds of General Formula (I).

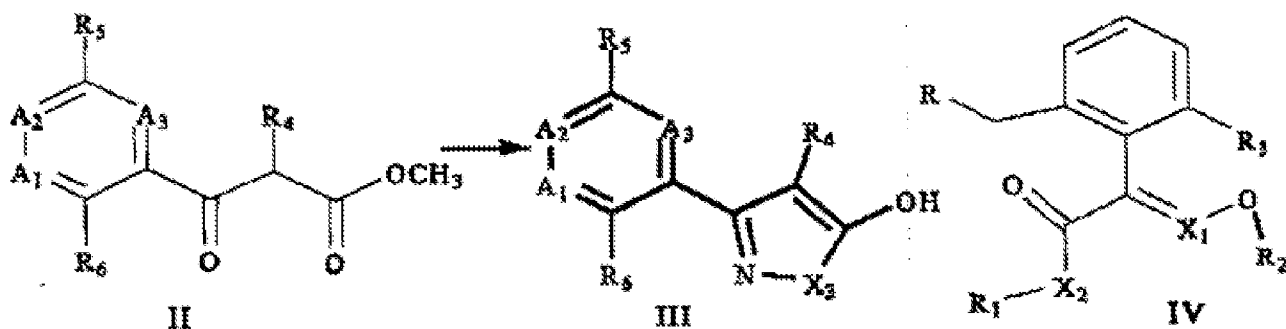
The compound and the stereoisomer of General Formula (I) are prepared by reacting azole compounds containing hydroxy groups, as shown in General Formula (III), with halomethyl benzene or azole compounds containing hydroxy groups as shown in General Formula (IV) under the presence of a base:



within General Formula (IV), R is a leaving group, selected from chlorine or bromine. Other groups are as defined above.

Intermediates (III) can be prepared by reacting of Intermediate (II) with (substituted) hydrazine or hydroxylamine according to known methods.

Intermediate (II) can be bought or prepared according to known methods. Please see CN 1257490A. The compounds of General Formula (IV) can be prepared according to known methods. Please see USP4723034 and USP 5554578.



The reaction occurs within a solvent. A suitable solvent can be selected from tetrahydrofuran, acetonitrile, toluene, xylene, benzene, N, N-dimethylformamide, dimethyl sulfoxide, acetone, or butanone, etc.

A suitable base can be selected from potassium hydroxide, sodium hydroxide, sodium carbonate, potassium carbonate, sodium bicarbonate, triethylamine, pyridine, or sodium hydride, etc.

Within a suitable solvent and under the presence of a suitable base, the target product is processed and prepared after reacting Intermediate (III) and (IV) (X₂ is oxygen and R is Br or Cl) at a suitable temperature for a specific period of time. The suitable temperature refers to a temperature range from room temperature to the boiling point of solvent, typically 20 to 100°C. The reaction time is from 30 minutes to 20 hours, typically 1 - 10 hours.

Within General Formula (I), compounds of General Formula (I) wherein X₁ = N and X₂ = NH can be prepared easily by reaction of compounds of General Formula (I) wherein X₁ = N, X₂ = O with a methylamine solution.

The compounds of the present invention offer exceptional

/17

fungicidal activity. These compounds have penetration activity and can be used as soil and foliar fungicides. They may be used to control diseases in all sorts of plants. They are especially effective in the prevention of the following plant diseases: said compounds provide excellent control of cucumber downy mildew, cucumber grey mold, cucumber powdery mildew, tomato early blight, tomato late blight, phytophthora blight of pepper, grape downy mildew, grape white rot, apple ring rot, apple alternaria leaf spot, rice sheath blight, rice blast, wheat leaf rust, wheat leaf blotch, wheat powdery mildew, rapescleorotinirose, corn southern leaf blight.

The compounds of present invention have very good insecticidal and pesticidal activity, and may be used to prevent all sorts of plant-damaging insects.

The present invention also provides a composition of insecticides and fungicides. The active ingredients of said composition are the compounds of General Formula (I) and the stereoisomer thereof, wherein the active ingredients present are a total amount of 0.1 to 99% by weight.

The present invention also provides a preparation method for the compositions defined therein. The compounds of General Formula (I) and the carriers are mixed. This type of composition may be a single component compound or a mixture of compounds with several components.

The carrier of the present invention is a substance that satisfies the following requirements: it is easy to apply to the sites being treated for the carrier after it is prepared with the active components. For example, the sites could be plant, seed, or soil. Or, the sites could be convenient

for storage, transportation, or operation. The carrier could be solid or liquid, including the liquids which typically transform from a gas condition under pressure. And the carriers which are used in preparation are typically the carriers used in insecticidal and bactericidal composition compositions.

Suitable solid carriers include natural and synthetic clays and silicates such as diatomaceous earths, talcs, magnesium aluminium silicates, aluminium silicates (kaoling clay), montmorillonites and micas; calcium carbonate; calcium sulphate; ammonium sulphate; synthetic silicon oxides and synthetic calcium silicates or aluminium silicates; elements such as carbon and sulphur; natural and synthetic resins such as coumarone resins, polyvinyl chloride, and styrene polymers and copolymers; solid polychlorophenols; bitumen; and waxes such as beeswax or paraffin wax.

Suitable liquid carriers include water, alcohols such as isopropanol and alcohol; ketones such as acetone, methyl ethyl ketone, methyl isopropyl ketone, and cyclohexanone; ethers; aromatics such as benzene, xylene, and toluene; petroleum fractions such as kerosene and mineral oils; chlorinated aliphatic hydrocarbons such as carbon tetrachloride, tetrachloride ethylene, and trichloride ethylene. In general, mixtures of these different liquids are often suitable.

The compositions of insecticides and fungicides are typically formulated and transported in a concentrated form and then subsequently diluted by the user before application. The presence of small amounts of surfactant carriers facilitates this process of dilution. Thus

preferably at least one carrier in the compositions based on the present invention is a surfactant. For example, the composition may contain at least two carriers, whereby at least one of which is a surfactant.

A surfactant may be an emulsifier, a dispersant, or a wetting agent. It may be a nonionic or ionic surfactant. Examples of suitable surfactants include the sodium or calcium salts of polyacrylic acids and lignin sulphonic acids; the condensation products of fatty acids or aliphatic amines or amides containing at least 12 carbon atoms in the molecule with ethylene oxide and/or propylene oxide; fatty acid esters of glycol, sorbic alcohol, sucrose or pentaerythritol and condensations of these with ethylene oxide and/or propylene oxide; condensation products of fatty alcohol or alkyl phenols such as p-octylphenol or p-octylcresol, with ethylene-oxide and/or propylene oxide; sulphates or sulphonates of these condensation products; alkaline metal salts or alkaline earth metal salts, preferably sodium salts, of sulphuric or sulphonic acid esters containing at least 10 carbon atoms in the molecule, such as sodium lauryl sulphate, sodium secondary alkyl sulphates, sodium salts of sulphonated castor oil, and sodium alkylaryl sulphonates such as sodium dodecylbenzene sulphonate.

Examples of compositions and formulations based on the present invention are wettable powder, dustable powder, granule, aqueous solution, emulsifiable concentrate, emulsion, suspension concentrate, aerosol composition and fumigant. Wettable powder usually contains 25, 50, or 75% weight of active ingredient and typically contain in addition to solid inert carrier, 3-10% weight of a dispersant and, where necessary, 0-10% weight of stabilizers and/or other additives such as penetrants or stickers.

Dustable powder are usually formulated as a dust concentrate having a similar composition to that of a wettable powder but without a dispersant, and are further diluted with solid carrier so that the composition /18 typically contains 0.5-10% weight of the active ingredient. Granules are usually prepared to have a size between 10 and 100 BS mesh (1.676 - 0.152 mm), and may be manufactured using agglomeration or impregnation techniques. Generally, granules contain 0.5-75% weight active ingredient and 0-10% weight of additives such as stabilizers, surfactants, and slow release modifiers. The so-called "dry flowable powder" is composed of a relatively high concentration of active ingredients in a relatively small granule size. Emulsifiable concentrates typically contain, in addition to a solvent and, when necessary, co-solvent, 1 - 50% W/V active ingredients, 2 - 20% W/V emulsifiers and 0 - 20% W/V of other additives such as stabilizers, penetrants, and corrosion inhibitors. Suspension concentrates usually contain 10 - 75% weight active ingredient, 0.5 - 15% weight dispersing agents, and 0.1 - 10% weight other additives such as defoamers, corrosion inhibitors, stabilizers, penetrants, and stickers.

Aqueous dispersant and emulsions such as compositions obtained by diluting a wettable powder or a concentrate based on the present invention with water, also fall within the scope of the invention. The said emulsions may be of water-in-oil or of oil-in-water types.

Compositions for which one or more types of fungicides are added have a wider spectrum activity than single compounds from General Formula (I). In addition, other fungicides may have a synergistic effect on the

fungicidal activity of compounds of General Formula (I). Compounds of General Formula (I) can also be used with other insecticides, or used with another fungicide and other insecticides simultaneously.

Preferred Embodiments

The following preferred embodiments further describe the present invention.

Synthesized Embodiments

Example 1: The preparation of Compound 2

Dissolve 2.12 g of ethyl 3-(4-chlorophenyl)-3-oxopropanoate in methanol. Heat the solution to reflux. Drip in slightly excessive methyl hydrazine to the solution and reflux for 3 hours. After the reaction is traced using TLC, the solution is then condensed, cooled, and the crystals are obtained. Filter and wash the crystals with methanol. Dry to obtain 1.5 g of crystal 3-(4-chlorophenyl)-1-methyl-5-pyrazol alcohol.

Dissolve 1.04 g of the aforementioned 3-(4-chlorophenyl)-1-methyl-5-pyrazol alcohol crystal in 5 ml of N, N-dimethylformamide. Add in 0.36 g sodium hydride and stir for 0.5 hours. Add in 1.42 g of methyl (*E*)-2-[2-(bromomethyl) phenyl]-3-methoxyacrylate. It is oil soluble at 40°C. Stir for 3 hours. After the reaction is traced using TLC the reaction mixture is poured into a 50 ml brine solution and extracted three times using 100 ml ethyl acetate. Dry, concentrate, and purify with column chromatography to obtain 1.3 g of the viscous oil product.

Example 2: The preparation of Compound 69

Add 0.15 g of sodium hydride to a reaction flask. After washing with petroleum ether, add 5 ml N, N-dimethylformamide. Then, add 3-(6-chloropyridin-3-yl)-1-methyl-5-pyrazol alcohol nitrobenzoyl ethyl acetate (0.5 g) which is prepared according to CN1257490A. Stir at room temperature for 2 minutes and then add in 0.7 g of methyl (E)-2-[2-(bromomethyl) phenyl]-3-methoxyacrylate. Stir and react at 60°C for 2 hours. After the reaction is traced using TLC, pour the reaction mixture into a 50 ml brine and extract three times using 100 ml ethyl acetate. Dry, concentrate, and purify with column chromatography to obtain 0.8 g of the light yellow solid.

Example 3: The preparation of Compound 86

Dissolve 2 g of nitrobenzoyl ethyl acetate in methanol and add in slightly excessive hydroxylamine hydrochloride and equivalent mol amount of sodium hydroxide. Then, heat and reflux for 3 hours. After the reaction is traced using TLC, add water and extract with ethyl acetate. Dry and concentrate to obtain 1.5 g solid 3-(4-nitrophenyl) isoxazol-5-ol.

Dissolve 1 g of the aforementioned crystal in DMF, add 0.4 g of sodium hydride, and stir for 0.5 hours. Add 1.4 g of methyl (E)-2-[2-(bromomethyl) phenyl]-3-methoxyacrylate. It is oil soluble at 50°C. Stir for 6 /19 hours. After the reaction is traced using TLC, pour the reaction mixture into a 50 ml brine and extract three times using 100 ml ethyl acetate. Dry, concentrate, and purify with column chromatography to obtain 1.5 g of the solid product.

The other compounds are also synthesized in the same manner.

Embodiments of Preparation

Example 4: 60% wettable powder

Compound 69	60% (weight)
Sodium dodecyl naphthalenesulfate	2% (weight)
Sodium lignosulfonate	9% (weight)
Kaolin clay	complement to 100% (weight)

Each component (all being solids) are well mixed together and ground in a grinder until the particle size reaches the standard.

Example 5: 35% emulsion concentrate

Compound 2	35% (weight)
Phosphorous acid	10% (weight)
Ethylenoxy aliphatic acid glycerin ester	15% (weight)
Cyclohexanone	complement to 100% (weight)

The phosphorous acid is dissolved in cyclohexanone, then Compound 1 and ethylenoxy aliphatic acid glycerin ester are added to obtain a transparent solution.

Example 6: 30% aqueous suspension

Compound 287	30% (weight)
Sodium dodecyl naphthalenesulfate	4% (weight)
Hemicellulose	2% (weight)
Epoxypropane	8% (weight)
Water	complement to 100% (weight)

The mixture of Compound 287 and 80% of the amount of water are added in a mill (1 mm ball) with the sodium dodecyl naphthalenesulfate and ground together. Other components are dissolved in the remaining water and added to the other components while stirring.

Example 7: 25% suspension emulsifier

Compound 12 25% (weight)

Alkylsulphonates (Emulsifier 1) 4 % (weight)

Ethylenoxy aliphatic acid glycerin ester (Emulsifier 2) 2% (weight)

Calcium dodecylbenzenesulfate (Emulsifier 3) 1.5% (weight)

Polyethylenoxyalkyl propyl ether (dispersant) 2.5% (weight)

Cyclohexanone (Solvent 1) 30% (weight)

Petroleum fractions (boiling point > 200°C) (Solvent 2) complement to 100% (weight)

Dissolve Compound 12 in 80% of the amount of solvent. And then, add in the emulsifiers and dispersant. Thoroughly stir the mixture. Grind the mixture in a mill (1 mm ball) and then add the remaining solvents.

Determination of Biological Activity

/20

Example 8: Determination of fungicidal activity

Determination of the fungicidal activity of using the compounds of the present invention against plant diseases was performed. The testing procedure was as follows:

Place the plant samples in a pot. Dissolve the compounds to be tested in a small amount of N, N-dimethylformamide. Dilute with water to the required concentration. Spray the test solution directly on the plants. Perform pathogen inoculation after 24 hours. After inoculation, place the plants in growth chambers under constant temperature and moisture so that the disease will continue to spread. Once the control group of plants exhibited full severity of the disease (typically after 1 week), inspect and evaluate.

Part of the test results are as follows:

At 500 pp [sic], Compounds 1, 2, 4, 5, 12, 69, 83, 84, 86, and 287, etc. showed 100% effectiveness against cucumber downy mildew and wheat powdery mildew.

At 100 ppm, Compounds 1, 2, 4, 5, 69, 84, 86, and 287, etc. showed 100% effectiveness against cucumber downy mildew and wheat powdery mildew.

At 100 ppm, Compound 2 showed more than 80% effectiveness against apple ring rot, wheat head blight, rape sclerotiniose, grape white rot, apple alternaria leaf spot, tomato early blight, tomato late blight, corn southern leaf blight, and grape downy mildew.